easy matter in infancy. It has practically no effect when given by the mouth. Strychnin is, in general, the most useful of the stimulants, while caffein and camphor are the best quick stimulants. Strychnin may be given in doses of from $\frac{1}{1000}$ to $\frac{1}{200}$ grain. The dose of the citrate of caffein by mouth for a baby is from 0.125 to 0.5 grain, and of caffein-sodium benzoate or salicylate subcutaneously about the same. Camphor may be given subcutaneously in oil in doses of from 1 to 2 grains.

THE DAMAGE DONE BY PYELOGRAPHY.[1]

By Edward L. Keyes, Jr., M.D.,
PROFESSOR OF GENITO-URINARY SURGERY IN THE CORNELL UNIVERSITY MEDICAL COLLEGE, NEW YORK.
AND
Herbert Mohan, M.D.,
NEW YORK.

(From the Pathologic Laboratories of Bellevue Hospital.)

At the present day we are all familiar with the lesions of the renal parenchyma due to injection of collargol, or similar substances, into the pelvis of the kidney for pyelography.

The pathological picture presented by such a kidney may be briefly described as follows: The surface of the organ usually shows black patches of collargol infiltration. These patches are slightly elevated above the surrounding tissue. They consist of a swollen parenchyma, irregularly mottled with black infiltrate. The capsule when stripped back, shows a replica of this staining.

On section we find that these patches, seen on the surface of the kidney, correspond to an underlying infiltrated area. Such an area is a black mottling or striation of the parenchyma, with intervening uninfiltrated spots. It may be irregular in outline, but often it is definitely cone-shaped, with apex at the pelvis and base at the capsule.

The pelvis itself is more or less stained and infiltrated. The cellular tissue about the pelvis may be stained black. The collargol is found within the tubules and the glomeruli. Moreover, masses of collargol, small or large, are found scattered between the tubules. The kidney tissue about such masses is likely to be inflamed or necrotic. The arteries and veins contain collargol.

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[1] Read in part before the American Association of Genito-urinary Surgeons, May 16, 1914.

In the two fatal cases of Roessle[2] and von Hoffmann,[3] death was apparently due, in the one to spesis, in the other to rupture of the pelvis of the kidney, with perirenal extravasation of the collargol and urine.

E. O. Smith[4] reports the death of a feeble, aged women five minutes after injection of 20 c.c. of collargol, causing pain. Autopsy showed emphysema, bronchiectasis, aortic sclerosis, arteriosclerosis, empyema of gall-bladder, nephritis, etc. Collargol was found in and between the renal tubules and in the epithelium.

Two explanations have been offered to explain the entrance of collargol into the kidney.

Blum, Oehlecker, and Tennant,[5] experimenting with cadaver kidneys, or kidneys removed from animals, independently reached the same conclusions, viz., that the collargol enters the tubules of the kidney and either passes up these to the glomeruli or breaks from a tubule into the interstitial tissue and so passes along the lymph spaces to the capsule.

Strassman, on the other hand, experimented with living rabbits. He exposed the kidney and ureter, and made his injections very gently, so as not to distend the pelvis unduly. The collargol was retained for varying lengths of time (eight minutes to twenty-four hours). His experiments did not produce infarcts, left no collargol in the kidney tubules, and showed that the collargol reached the kidney capsule *via* the bloodvessels and lymphatics and the connective tissue around the urinary canals. He therefore denies rupture of the tubules or even distention of them.

Strassman's conclusions have been criticised by both Mason and von Hoffmann on the score of neither fulfiling the clinical condition (distention of the renal pelvis to the point of colic) nor exhibiting the pathological lesions resulting therefrom (distention of the tubules).

But sufficient stress has been laid on the importance of not overdistending the renal pelvis. Everyone now realizes that even 10 c.c. is much too large a quantity to inject into some pelves; 5 c.c. is the usual limit; and the safety of gravity injection as compared with syringe injection is accepted. Moreover the lesions resulting from too large an injection have been studied by many, notably by Eisendrath.[6] But we have reason to believe that injection of the renal pelvis *without* distention may damage the parenchyma. The following experiments have been undertaken for the purpose of studying the nature of this damage and of verifying Strassmann's observations:

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[2] Münch. med. Woch., 1911, No. 5.

[3] Folia Urologica, February, 1914, viii, 393.

[4] Trans. Amer. Urolog. Assoc., 1913, vii, 36.

[5] Mason, Jour. Amer. Med. Assoc., March 14, 1914, lxii, 839, has brought the bibliography up to date.

[6] Genito-urinary Section, Amer. Med. Assoc., 1914.

Experiment 1. The upper part of the ureter and the kidney of a dog were exposed through an abdominal incision. One c.c. of 10 per cent. collargol solution was then injected into the pelvis. This amount of fluid seemed to distend the pelvis *without putting it under tension*. The needle was *immediately* withdrawn and the kidney removed.

The kidney was hardened and stained in the usual manner. Externally it did not appear congested and no collargol was seen under the capsule or in the cellular tissue about the pelvis.

On section the pelvis was seen to be lightly stained with collargol and a few minute black spots could be seen in the cortex.

Microscopically the pelvis showed a coating of collargol. The parenchyma was almost entirely normal, but traces of collargol were found, apparently in lymph spaces, near the periphery of the cortex. There was no trace of collargol found in the tubules, the glomeruli, or the bloodvessels of the pelvis or parenchyma.

Experiment 2. The opposite kidney of the same dog was simultaneously exposed and injected *in the same manner*, with the exception that the pelvis was kept *distended for fifteen minutes*. The kidney was then removed and the dog killed before he recovered from the anesthetic.

The gross appearance of this kidney was the same as that of the first experiment, with the exception that the pelvis was more deeply stained and the parenchyma showed many black spots, while the veins outside of the kidney were somewhat distended.

Microscopically the pelvic was coated with collargol, which was also found in considerable quantity in the bloodvessels adjacent to the pelvis and to a less degree in the vessels and lymph spaces within the parenchyma. There were distinct but slight traces of collargol in the glomeruli, and either in the epithelia or in the lumina of the tubules.

Experiment 3. The dog used for this and the following experiment was considerably larger than the one previously employed. Accordingly 2 c.c. were injected to produce an approximately corresponding degree of distention of the pelvis. A 2 per cent. solution of collargol was employed. The pressure was *immediately released* and the dog *killed twenty-four hours later*.

The kidney was markedly congested and there was hemorrhage into the cellular tissue about the pelvis within the hilum; but no trace of collargol was found on inspection, either in the pelvis or in parenchyma.

The microscope revealed acute congestion of the kidney, with considerable dilatation of the vessels and parenchymatous hemorrhages; but no collargol in the pelvis, the vessels, or the glomeruli and only a very few faint traces of collargol in the tubules.

Experiment 4. The opposite kidney of the same dog was injected in like manner, but the distention was maintained for *fifteen minutes.* This kidney was removed with its fellow twenty-four hours later.

The gross external appearance was similar to that of the preceding experiment, with the exception that the veins running over the kidney were more congested, the kidney rather browner.

Section revealed a black staining of the surface of the pelvis and black infiltration of the cellular tissue about the pelvis. Many small black spots were also visible throughout the parenchyma.

Microscopically the kidney showed a congestion somewhat less intense than that found in Experiment 3 and a collargol distribution similar to, but more marked than, that of Experiment 2.

The collargol in the parenchyma, while still showing marked affiliation for the bloodvessels, was also seen (and in rather greater quantity than in Experiment 2) in the glomeruli, and distinctly both in the epithelia and in the lumina of the tubules.

From these experiments, few though they be, we derive the following conclusions:

1. Momentary gentle distention of the normal pelvis of the kidney doubtless causes no more damage than a congestion of the organ (Experiments 1 and 3), which congestion is doubtless of brief duration.
2. But if the distention persists for a few minutes the injected fluid is absorbed into the bloodvessels and lymph spaces about the kidney pelvis.
3. Although, like Strassmann, we have been unable to detect any collargol forced into the collectiong tubules;
4. Nevertheless, we have found collargol in the glomeruli and in the convoluted tubules.
5. But inasmuch as there was much less collargol within the glomeruli and tubules than in the lymph spaces and vessels.
6. We conclude that the appearance of the collargol within the glomeruli and tubules is a secretory phenomenon.

SECONDARY OR LATE INFILTRATION. Such are the immediate results of slight distention of the normal kidney pelvis. But a case reported by von Hoffmann introduces a new point, for in this case death resulted from rupture of the pelvis, although at the time of collargol injection the patient had not the least pain in the kidney. *The pain came on for the first time twenty minutes after the examination.*

The history of this case is, briefly, as follows: The patient was fifteen years of age, and had had digestive symptoms for five years and colics in the left loin for a year and a half. There was an intermittent tumor in the left loin. Infected intermittent hydronephrosis was diagnosed. Ureter catheterization revealed a marked delay in indigo-carmine secretion from the left kidney and pus from this side. A 5 per cent. solution of collargol was injected slowly through the ureter catheter until it regurgitated into the bladder.

The catheter was left in place for ten minutes after injection, during which time a considerable amount of collargol issued from it, and the patient felt no pain in his side, but complained of a good deal of bladder pain. Half an hour later he had severe left renal colic and vomited. Four days later he died, the pains having continued and grown more severe, the pulse being rapid, the tongue dry, the temperature low. Postmortem examination revealed hydronephrosis of the left kidney, pyelonephritis, abscess in the parenchyma, infiltration of the parenchyma with collargol, and a ruptured pelvis which had caused death.

Since the patient did not have any pain in the kidney at the time of the injection, the infiltration of the kidney parenchyma as well as the death of the patient were due to obstruction of the ureter subsequent to catheterization. The excretion of urine into the hydronephrotic sac was doubtless the cause of pain, infiltration, rupture, and death.

We shall now report a personal observation: The patient, an Italian laborer, aged seventeen years, entered St. Vincent's Hospital in October, 1913. Apart from the common diseases of childhood he gave no history of any significance, excepting that of his present malady. This consisted in attacks of severe pain in the left loin, radiating downward toward the groin. These pains first began in 1910, following a severe lifting strain. They varied in frequency, duration, and severity; but were usually very intense, lasting about two days, and occurring about six times a year. He had never noticed any disturbance of urination or the passage of stone or blood in the urine. The attacks were not accompanied by any recognized fever, but were associated with nausea. He entered the hospital with no definite diagnosis, his physician even asserting that the left kidney could not be felt. But careful examination of the left loin revealed an obscure general thickening of the loin without any definite outline, tenderness, or muscular rigidity. This was assumed to be a large, empty, hydronephrotic sac. Urinalysis revealed an adequate output of urea, a few pus cells, a trace of albumin (and clumps of bacilli that were acid fast when decolorized for a brief period).

October 27. Cystoscopy showed a normal bladder and normal ureter orifices. Ureter catheters passed readily to the kidney pelvis on the right side, but only 10 cm. up the left ureter. From this left side a gush of some 20 to 30 c.c. of urine was immediately obtained, as though from a dilated ureter. The urine obtained from the right side showed 2.8 per cent. urea and no pus. That from the left side showed 1.2 per cent. urea and a few pus cells. Phenolsulphonephthalein came down strongly from the right side and very faintly from the left (but the precise data of this have unfortunately been lost).

Fifteen c.c. of 25 per cent. cargentos were injected into the left ureter. Radiographs were then taken; those of the left loin failing to show the kidney or any trace of the injected fluid; those of the bony pelvis showing the left ureter filled with cargentos up to the pelvic brim and enormously dilated.

The patient complained of no unusual pain from the cystoscopy and felt *no pain in the loin either during the injection or subsequent to it.*

In the two days that intervened between the injection of the left ureter and the removal of the kidney the temperature rose to 101°, and the left kidney became distinctly distended and notably sensitive; but still the patient had no spontaneous pain whatever in the left side.

October 29. Although there was still grave doubt as to the presence of real tubercle bacilli, it was evident that the kidney would have to be removed, whether tuberculous or not, since the organ itself was evidently almost entirely destroyed and the ureteral obstruction was near the lower end of the ureter. Accordingly nephrectomy was performed.

The kidney was very large and the adhesions about the vessels so dense that it was deemed prudent to leave clamps on them. The operation was concluded in forty-five minutes.

The postoperative history was uneventful. The clamps were removed on the third day. The patient left the hospital on the fifteenth day with his loin healed.

To my great surprise the kidney showed the typical lesions of injection infiltration (Fig. 1). Indeed the capsule was stained with the injected fluid over an unusually large area. Section revealed the familiar gross lesions and a greatly dilated pelvis containing a brownish dilute solution of cargentos.

Microscopic section of the kidney revealed ulceration of the pelvis and extensive areas of suppuration and sclerosis in the parenchyma, while the remaining tubules and glomeruli showed the familiar lesions of suppuration and dilatation. The cargentos were found distributed irregularly throughout the kidney. There were many infiltrated areas containing granular black deposit. Many glomeruli contained back granules in considerable quantity, and here and there the tubules were filled with black deposit. These lesions do not differ from those that have been described in similar specimens.

This case illustrates much more clearly the point suggested by the case of von Hoffmann, for our patient had no pain at any time. Yet the ureter was evidently completely blocked as a result of the injection, the kidney gradually filled, and the patient would have had a renal colic if operation had not been promptly performed. Yet meanwhile, without any colic, and with pressure of urinary secretion only strong enough to distend the kidney moderately, the classical infiltration took place. This is, therefore, an example of what might be called secondary infiltration of the kidney parenchyma subsequent to injection, in constrast to primary infiltration at the time of injection.

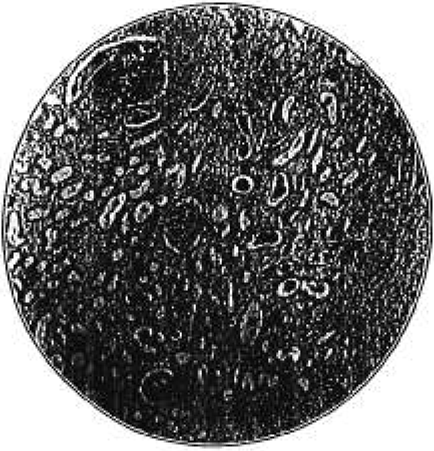

FIG. 1.—Infected hydronephrosis, showing the distribution of collargol in glomeruli and tubules, and the association of collargol with areas of hemorrhage and necrosis (human).

That there is a primary infiltration at the time of the injection, and caused by too forceful dilatation, we cannot doubt. It has been illustrated in many cases, notably by the case of Zachrisson. This patient received an injection of 14 c.c. of collargol into a normal pelvis of the kidney, and the roentgen-ray, taken immediately thereafter, showed a pyramidal shadow of collargol radiating into the parenchyma of the kidney.

After five days of pain and fourteen days of fever he recovered. The *opposite* kidney was subsequently removed and a year thereafter the urine showed nothing abnormal excepting a few casts. Postmortem examination of Smith's patient revealed a similar condition.

These cases illustrate the fact that immediate infiltration can take place. Yet secondary infiltration is perhaps more common than has been supposed. Primary infiltration is certainly painful and must doubtless result in considerable destruction of kidney tissue; but so long as focal suppuration does not follow and the ureter remains open the patient may be expected to recover. Indeed, Smith's is the only recorded immediate death.

Secondary infiltration is obviously a far more serious accident. If the kidney is not promptly drained or removed the ureter may remain closed and the pelvis rupture, as in von Hoffmann's case. Whenever an injection is made into the pelvis in a case of renal retention the patient must, therefore, be kept under close observation and promptly operated upon if symptoms of acute renal retention or infection supervene. Thus will the real danger of pyelography be guarded against.

How does the injected fluid enter the parenchyma in these cases of secondary infiltration? Why does secondary infiltration occur? If the injected collargol may be forced up to the capsule under no other force than that of the urine secretion itself we must conclude that a similar condition of infiltration of the kidney parenchyma with urine must occur in many, if not in all, cases of severe renal colic. Does such an infiltration occur? And if so, is it an element in the etiology of hydronephrosis? Furthermore it is interesting to inquire whether the pathological picture presented by a kidney subjected only to primary renal infiltration differs from that of a kidney subjected only to secondary renal infiltration?

Although we cannot pretend to answer these questions with any degree of thoroughness, we have performed some experiments on dogs which throw an interesting light upon them.

Experiment 5. The whole length of the ureter of a dog was exposed through an abdominal incision and 3 mgs. of 2 per cent. collargol were injected into the lower end of the ureter. The black fluid could be plainly seen ascending the ureter. As soon as it reached the pelvis, and before any dilatation of the pelvis occurred, the injection was stopped and the ureter tightly ligated with silk just above the point of injection. The abdominal wound was then closed and the kidney removed twenty-four hours later. This kidney showed exactly the same changes as that of Experiment 4, with the exception that grossly a considerable amount of collargol showed beneath the capsule. On the other hand, microscopically, this kidney showed rather less collargol in the glomeruli than did kidney 4.

The object of this experiment was to simulate, as closely as possible, a secondary retention. The pelvis of the kidney was certainly not in the least distended at the time of the injection, but the collargol was left in the ureter so as to show the effect of the kidney secretion in producing auto-infiltration. The fact that the pathological changes produced were quite the same as those of experimental primary retention, suggests that in normal kidneys, at least, secondary as well as primary collargol infiltration is a vascular and lymphatic absorption, and that the collargol seen in the glomeruli and tubules is simply being excreted.

In order to confirm this impression the following experiment was performed:

EXPERIMENT 6. The whole left ureter of a dog was exposed, as in the preceding experiment, and 0.25 c.c. of a 10 per cent. collargol solution injected into its lower end, while the upper end was compressed in order to make certain that no collargol whatever entered the pelvis of the kidney. Pressure was immediately released from above and the lower end of the ureter ligated. Seventy-two hours later the dog was killed and both kidneys removed.

The injected left kidney was moderately congested and slightly larger than its fellow. Stained areas of parenchyma could be seen through the capsule. On section the pelvis was found dilated and filled with a muddy fluid, while minute black spots were visible throughout the parenchyma.

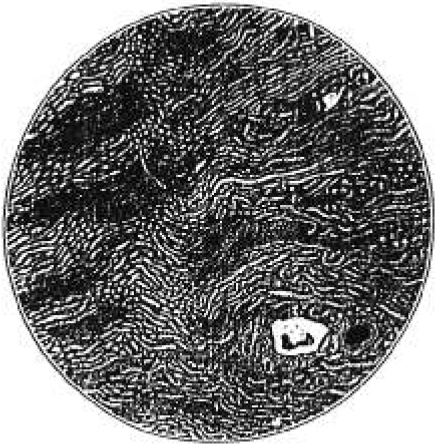

FIG. 2.—Collargol in vessels and in and between tubules, associated with areas of hemorrhage and infiltration (dog).

On microscopic section the most striking characteristic was the association of collargol and blood, both within the vessels and in many small hemorrhages scattered throughout the parenchyma.

Many convoluted tubules of the cortex and many straight tubules of the medulla showed collargol stained epithelia. About such tubules there were hemorrhages containing collargol (Fig. 2). Collargol was found free in the lumina of some straight tubules and also in some of the glomeruli.

The uninjected right kidney showed some congestion, but less than the left. No collargol was visible upon its surface, but section revealed numerous minute black spots in the cortex.

The microscope revealed much less collargol than in the injected kidney. The collargol was found exclusively in the vessels and the glomeruli. The latter contained much more collargol than did the glomeruli of the injected kidney.

This experiment thus afforded ample experimental confirmation of vascular absorption (left kidney) 'and glomerular excretion (right kidney).

Our next effort was to perform a similar injection upon a hydronephrotic kidney.

EXPERIMENT 7. Accordingly the left ureter of a dog was tied off with silk just above the bladder. (The parietal wound became infected, but this did not interfere with the result). One week later the kidney was exposed and found hydronephrotic. The dilated left ureter was punctured, 10 c.c. of urine were permitted to escape, and 3 c.c. of a 10 per cent. collargol solution injected, leaving the kidney distinctly less distended than it had been in the first place. The ureter was again ligatured and the wound closed. Forty-eight hours later the dog was killed and both kidneys removed.

The injected left kidney was markedly dilated and its surface studded with small raised areas of suppuration. The surface of the lower pole, the upper end of the ureter and the fatty tissue about the hilum were stained a deep black; and small black areas were seen beneath the capsule in other parts of the kidney. On section a large quantity of muddy fluid escaped from the distended pelvis, and the parenchyma showed many small black spots.

Microscopically this kidney showed so much suppuration that very little normal kidney tissue remained. But throughout the section the blood, whether extravated or within the vessels, was almost everywhere mingled with collargol. In the medulla streaks of hemorrhage and collargol paralleled each other in the general direction of the collecting tubules (Fig. 3).

The opposite (right) kidney showed no collargol upon its surface, but section revealed many black spots in the cortex. The microscope revealed collargol in the cortical bloodvessels, and in the glomeruli as well (Fig. 4). No collargol was found in the tubules or anywhere in the medulla.

These experiments appear to justify the following additional conclusions:

7. In actual practice we have to consider a secondary infiltration due to renal retention following the examination.

8. This secondary distention is of far greater importance than the primary retention at the time of injection.

9. Secondary retention is the cause of most of the deaths that have been reported from pyelography.

10. The cause of infiltration in these cases is ureteral obstruction. Hence it may occur when there has been no primary distention.

11. Alarming symptoms following pyelography are to be relieved by immediate drainage of the kidney or nephrectomy.

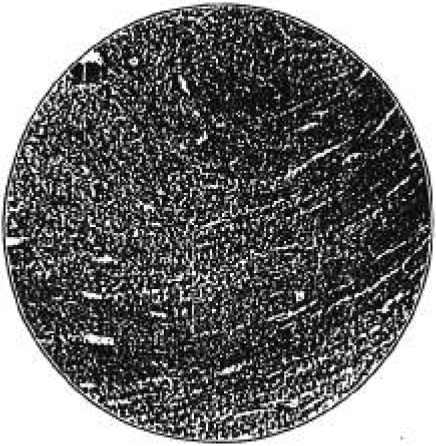

Fig. 3.—Infected hydronephrosis, showing collargol in glomerulus, and associated with an area of hemorrhage and infiltration both inside and outside the straight tubules (dog).

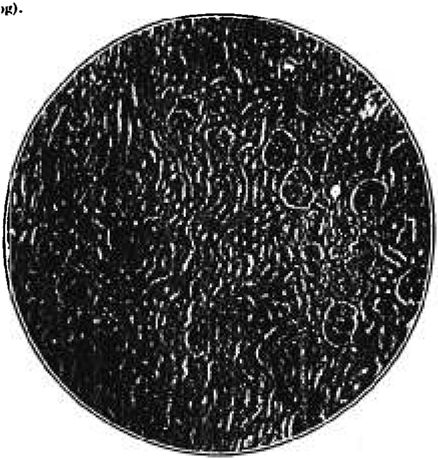

Fig. 4.—Lesions due to excretion of collargol in kidney opposite one injected. Many glomeruli contained collargol (dog).

12. The presence of collargol in the kidney parenchyma, as shown by radiograph or by operation, should not be a cause of apprehension, though it shows that the injection has been made with too much force.

13. The collargol may enter the general circulation and be distributed to the other kidney and elsewhere, in some instances at least, and yet no great harm result.

THE RESULTS AND INTERPRETATION OF THE WASSERMANN TEST.[1]

By Charles F. Craig, M.D.,
CAPTAIN MEDICAL CORPS, U. S. ARMY.

(From the Department Laboratory, Central Department, U. S. Army, Fort Leavenworth, Kansas).

In the present paper I shall give a summary of the present status of the Wassermann test in the diagnosis and as a control of the treatment of syphilis together with some data of practical value derived from personal experience with the test. The statistical portion of the paper is based upon over 18,000 tests personally performed by me, partly at the laboratory of the Army Medical School, Washington, D. C., and partly at this laboratory during the past five years.

It has now been over eight years since Wassermann, Neisser, and Bruck[2] published their description of what is now generally known as the Wassermann test, and during this time the test has been given a thorough trial in all parts of the world, with the result that the consensus of opinion is that, all in all, it is the most valuable aid that we possess in the diagnosis of syphilis. Certainly, my own experience has convinced me that, when properly performed, this test is of inestimable value not only in the diagnosis of the disease, but as a control of the efficiency of treatment. A positive reaction with the Wassermann test is the most delicate and persistent of all of the symptoms of syphilis, and it is irrational to consider a patient as cured of the disease so long as either the blood or cerebrospinal fluid react positively. The theory, advocated by a few authors, that a positive Wassermann reaction is merely an evidence of past syphilitic infection, has been proved to be erroneous, and it is now generally admitted that a positive reaction, if persistent, means the presence somewhere in the body

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[1] Published with permission of the Surgeon-General, U. S. Army.

[2] Wassermann, Neisser and Bruck. Eine serodiagnostische Reaktion bei Syphilis Deut. med. Wochenschr., 1906, xxxii, p. 745.